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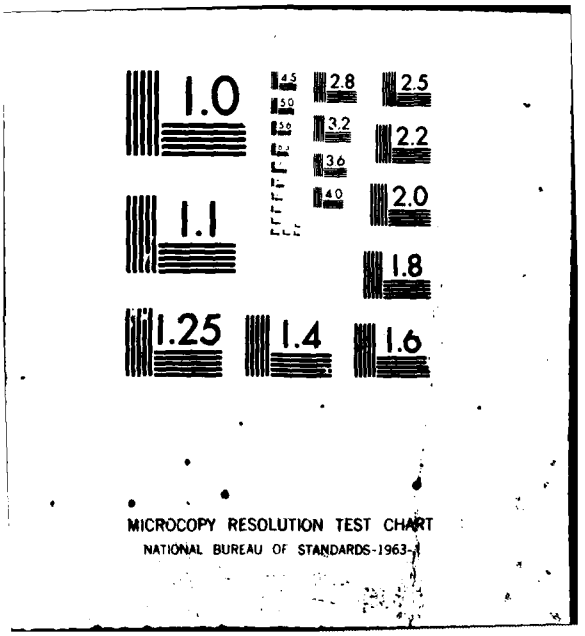
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MICROCOPY RESOLUTION TEST CHART
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Contract N00014-79-C-0076 new

Task No. NR 207-176

Technical Report No. 1

Navy Environment: Dielectric Studies of Biological Materials

by

Donald S. Kirkpatrick

The Institute for Rehabilitation and Research
1333 Moursund Avenue
Houston, Texas 77030

30 May 1980

ONR.1

FINAL REPORT

Technical Report No.1

Navy Environment: Dielectric Studies of Biological Materials

Our accomplishments under this contract include the following topics:

1. Data acquisition from time-domain reflectometer
2. Preparation of manuscript describing our preliminary dielectric spectroscopy of membrane suspensions
3. Preparation of manuscript for research proposal on dielectric spectroscopy of water-macromolecule interactions
4. Rheological investigation of cystic fibrosis mucus and preparation of manuscript

Each of these topics is discussed below.

1. Data Acquisition from Time-Domain Reflectometer

Data acquisition from the time-domain reflectometer by microcomputer became first priority in this project due to prolonged failure of our original data acquisition computer.

a. Selection of appropriate microcomputer

We selected a data acquisition computer to satisfy several criteria. We required more than 16K bytes of internal memory in order to accomodate simultaneously 2000 to 4000 data points (two bytes each) from each of two scans, viz., sample and reference scans. Sufficient external memory was needed to store scan pairs from multiple experiments. For this task we selected a Cromemco System II microcomputer with 32K bytes of random access memory and two 5 inch minifloppy disc drives. This instrument also provided both BASIC and FORTRAN IV for ease in computations as well as an assembler for data acquisition.

b. Time-domain reflectometer-computer interface

The data from the sampling oscilloscope consist of analog signals from its horizontal and vertical output terminals. These outputs represent the X-Y coordinates of the trace displayed on its screen. The sampling oscilloscope also generates from its pre-trigger output 3000 regularly spaced pulses per trace.

Our task was to provide the logic interface between the horizontal and pre-trigger outputs of the oscilloscope and the digital interface of the computer. This interface uses the pre-trigger output pulses from the oscilloscope to command acquisitition of each data point in the trace, and the

discontinuity of the horizontal ramp signal to initiate and terminate each trace. The data are acquired from the vertical output of the oscilloscope using a sample/hold amplifier to sample the analog signal followed by an analog/digital converter to digitize the sampled value. The computer then stores the value in memory. The logic interface allows program control of the data acquisition. There was no attempt to control the output of the oscilloscope by the computer.

The schematic diagram of the logic interface board is shown in following diagram along with the the timing diagram and flow chart for the data acquisition program.

2. Preparation of Manuscript: HYDRATION DEPENDENT, COLLECTIVE DIELECTRIC BEHAVIOR OF ROD OUTER SEGMENTS

ONR.2

We prepared a manuscript which reports our preliminary data on the dielectric behavior of membrane systems. This manuscript is summarized as follows.

SUMMARY

We observed in concentrated aqueous suspensions of rod outer segments a "slow" dielectric process with a relaxation time of about 10^{-8} s. The "slow" process was about 10^3 slower than the dielectric relaxation time of solvent water. The dielectric constant of the "slow" process 1.) varied with the hydration level of the suspension, reaching a maximum greater than 1000 in the hydration range which equaled the water content reported for rod outer segments *in vivo*, 2.) correlated with conductivity and ionic strength of the suspending solution, and 3.) was too large to be explained by linear combinations of water and membrane, which display dielectric constants of 78 and 2, respectively.

The following causes for the "slow" dielectric process were inconsistant with our observations: 1.) dipolar rotations of proteins in the plane of the membrane, 2.) membrane gating currents, and 3.) interfacial polarization, *viz.*, Maxwell-Wagner and frequency dependent, transverse conductance and capacitance. We suggest a collective or many-body interaction between water, ions, and membrane macromolecules to explain the magnitude of the dielectric constant, its dependence upon hydration, and its correlation with conductivity.

Copies of this manuscript have been submitted to the Program Director, Biophysics.

3. Preparation of Manuscript for Research Proposal: INVESTIGATION OF WATER-MACROMOLECULE INTERACTIONS BY DIELECTRIC SPECTROSCOPY ONR.4

This manuscript 1.) summarized our dielectric experiments, 2.) presented the experimental details of the time-domain (Fourier transform) dielectric spectroscopy technique, 3.) reviewed water-protein interactions, and 4.) presented a rationale for investigating water-protein interactions by dielectric spectroscopy. This manuscript has been submitted to the Program Director, Biophysics. It will be submitted to various foundations and institutes as a grant proposal in the future.

4. Rheological Investigation of Mucus ONR.3

We correlated physical and chemical properties of mucus in order to determine the chemical basis for mucus becoming obstructive in obstructive mucus diseases such as cystic fibrosis. A manuscript, SALIVARY MUCUS: CORRELATION BETWEEN FLOW PROPERTIES AND CHEMICAL PROPERTIES IN CYSTIC FIBROSIS SALIVA reported this work, and has been submitted to the Program Director, Biophysics. It is summarized below.

SUMMARY

In order to determine the chemical basis for mucus becoming obstructive, we simultaneously investigated both the rheological properties of mucus and its chemical composition. We estimated the value of Tow (tackiness or Spinnbarkeit) and quantitatively measured six chemical parameters of individual specimens of salivary mucus from cystic fibrosis patients. We found that we could describe the relationship between Tow and the chemical parameters by the multivariate equation:

$$Tow = 2.75(Alb.) + 0.456(T.Pro.) + 0.024(Cond.) - 1.241(T.Carb.) + 0.001(Amy.) + 0.355. \quad \text{(Equation 1)}$$

Equation 1 predicts the value of Tow from the chemical constituents of the mucus, viz., endogenous concentrations of albumin, total protein, inorganic ions (as measured by conductivity), total carbohydrate, and alpha-amylase. It is significant at the $p = 0.1$ level, and accounts for 25% of the variability observed in Tow (multiple R squared = 0.25). With more data points this relationship can become significant at the $p = 0.05$ level. Our data established for the first time that rheological properties of CF salivary mucus correlate with concentrations of its multiple chemical components.

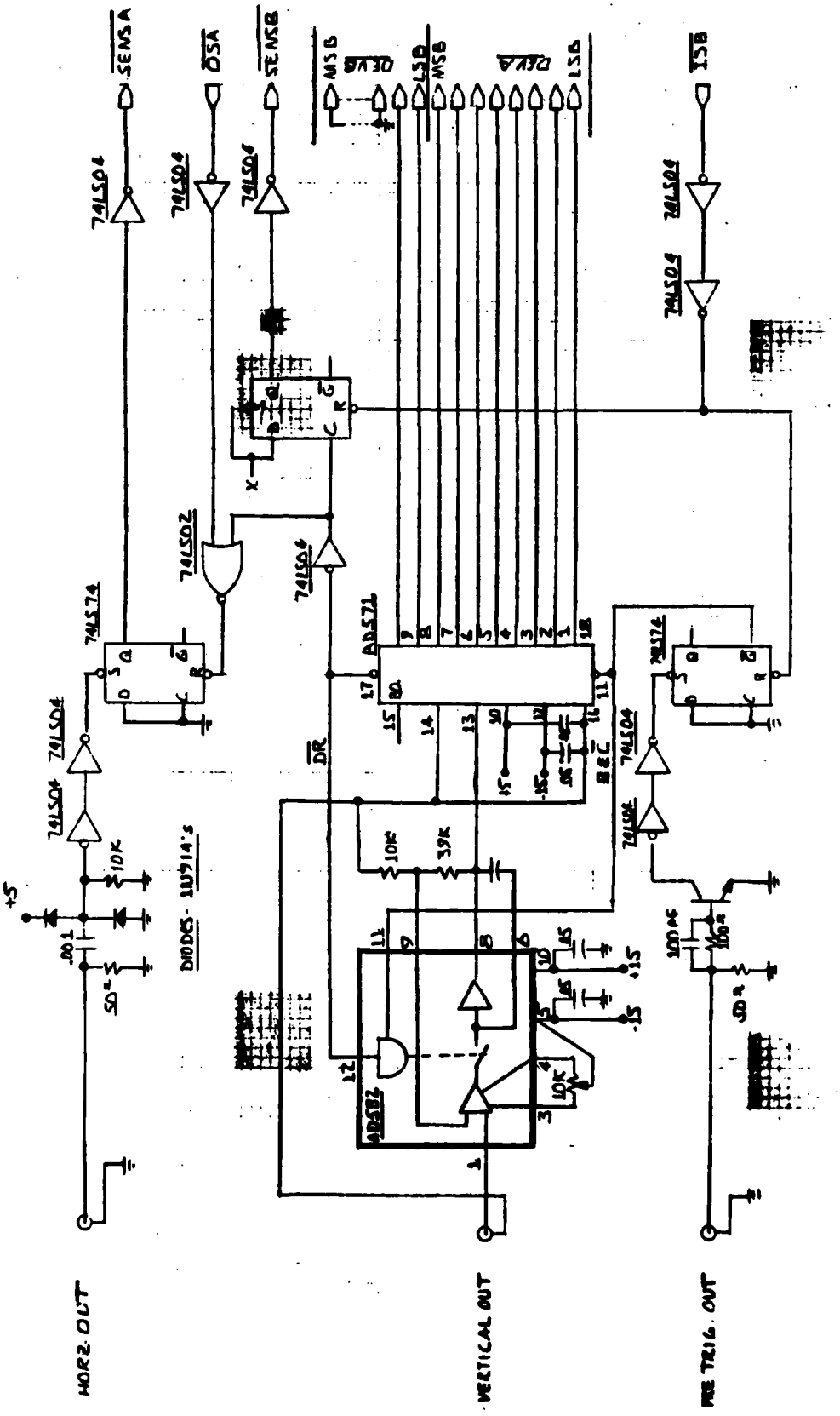
These correlations suggest roles for albumin, mucin glycoproteins, and inorganic ions in enhancing, and for unidentified carbohydrate containing material in diminishing, visco-elasticity of CF mucus. Equation 1 was independent of wide, week to week fluctuations, which we observed in both Tow and chemical parameters of individuals. Such fluctuations precluded correlation of Tow with the presence or severity of CF disease. Tow fluctuations probably resulted from the fluctuations which we observed in the concentrations of chemical constituents, rather than from possible fluctuations in mucin glycoprotein structure or function, as previously suggested.

Our preliminary results confirm the effectiveness of our strategy for investigating obstructive mucus. This strategy consists of simultaneously measuring both the rheological properties and the concentrations of multiple chemical constituents of individual specimens of CF salivary mucus. Their relationships are examined by multivariate analysis. On this basis we propose three immediate goals:

1.) Verify our preliminary results using good statistical design.
2.) Refine the original physical and chemical parameters of saliva to more specific and well defined parameters.
3.) Investigate the cause and effect relationships between rheological properties and chemical constituents, which the correlations suggest

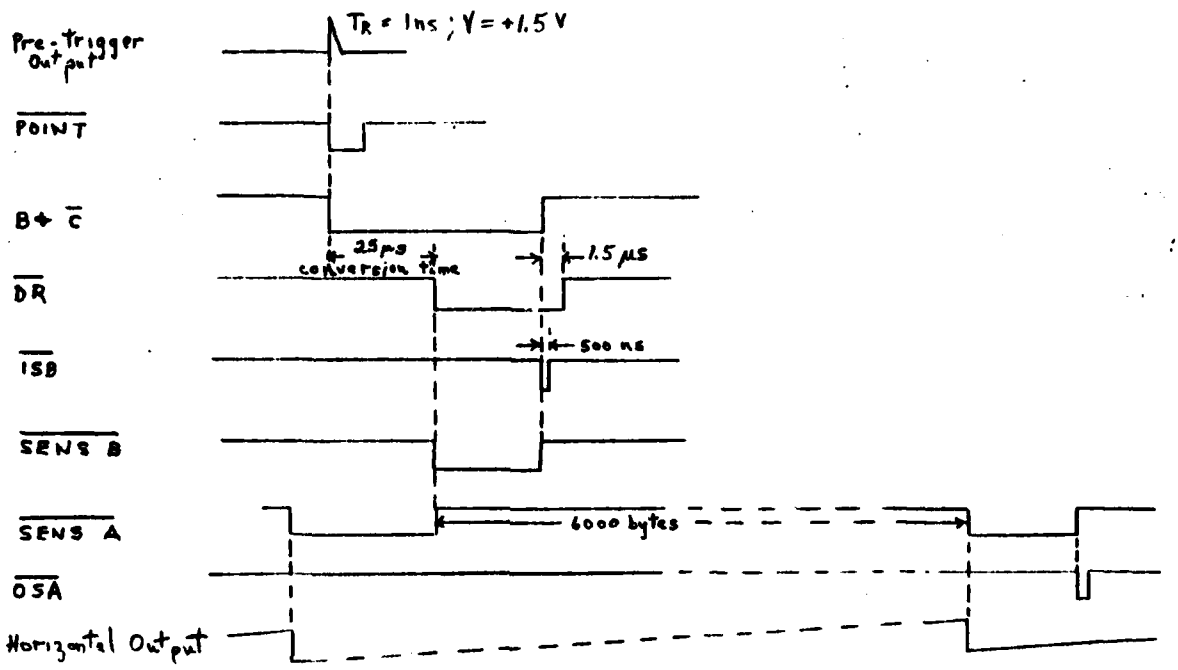
Following this strategy, we expect to determine how the rheological properties of mucus are physiologically regulated as well as how obstructive mucus can be managed clinically. We hope that this knowledge will enable us to prevent the fatal lung damage which CF inflicts.

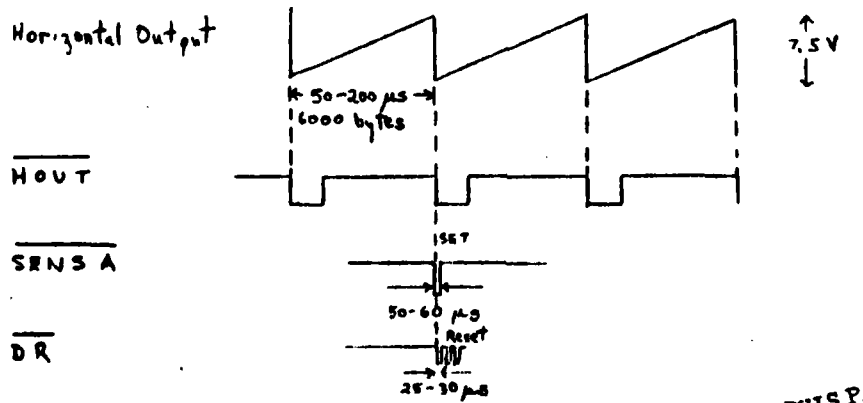
Logic Interface between Time-Domain Reflectometer and TU-ART Digital Interface (Cromemco)



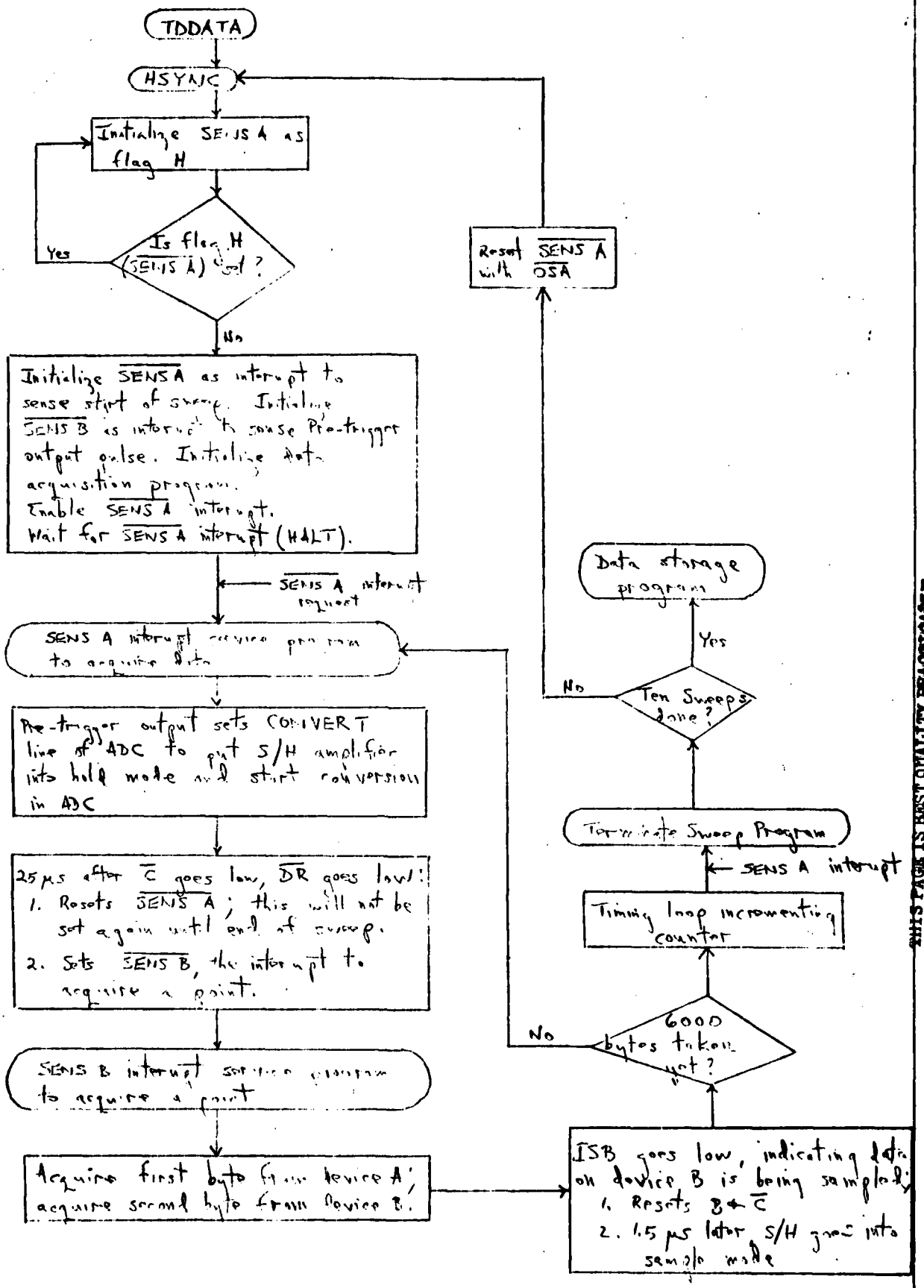
DATA ACQUISITION

Timing Diagram between Time-Domain Reflectometer and TU-ART Digital Interface (Cromemco)





Program Flow Chart for Data Acquisition from Time-Domain Reflectometer



(1) Final rept. 1 Nov 78-29 Feb 80

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: Technical Report No. 1.
2. GOVT ACCESSION NO.: AD-A085 223
3. RECIPIENT'S CATALOG NUMBER:

(6) 4. TITLE (and Subtitle): Navy Environment: Dielectric Studies of Biological Materials
5. TYPE OF REPORT & PERIOD COVERED: Final Report, Nov 1978 - Feb 29, 1980
6. PERFORMING ORG. REPORT NUMBER:

(10) 7. AUTHOR(s): Donald S. Kirkpatrick
(15) 8. CONTRACT OR GRANT NUMBER(s): N00014-79-C-0876

9. PERFORMING ORGANIZATION NAME AND ADDRESS:
The Institute for Rehabilitation and Research
1333 Moursund Ave.
Houston, Texas 77030

10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: RR-041-08-02

11. CONTROLLING OFFICE NAME AND ADDRESS:
Office of Naval Research Biophysics Program
Code 444

12. REPORT DATE: May 30, 1980
13. NUMBER OF PAGES: seven (7)

14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office):
Not different (14) TR-1

15. SECURITY CLASS. (of this report):
15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT (of this Report):
Distribution is unlimited
(16) RR041 08
(17) RR041 08 02

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report):
Distribution is unlimited
(11) 30 May 80

18. SUPPLEMENTARY NOTES
(12) 11

19. KEY WORDS (Continue on reverse side if necessary and identify by block number):
Dielectric, water, protein, membrane, many-body, mucus, rheology, mucin, glycoprotein, cystic fibrosis

20. ABSTRACT (Continue on reverse side if necessary and identify by block number):
We designed the logic interface and data acquisition program to acquire data for a Fourier transform dielectric spectrometer. We prepared three manuscripts: 1.) HYDRATION DEPENDENT, COLLECTIVE DIELECTRIC BEHAVIOR OF ROD OUTER SEGMENTS, which reports our preliminary dielectric spectroscopy of biological materials, 2.) INVESTIGATION OF WATER-MACROMOLECULE INTERACTIONS BY DIELECTRIC SPECTROSCOPY, a research proposal, 3.) SALIVARY MUCUS: CORRELATION BETWEEN FLOW PROPERTIES AND CHEMICAL PROPERTIES IN CYSTIC FIBROSIS MUCUS, which reports our rheological/chemical investigation of cystic fibrosis mucus.

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE
S/N 0102-LF-014-6601

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

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